OIPE JC174
JAN 30 2004
PATENT & TRADEMARK OFFICE

PATENT
Atty. Dkt. No. 023597-0110

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Gregory S. Hamilton et al.

Title: COMPOUNDS HAVING SIMULTANEOUS ABILITY TO BLOCK L-TYPE CALCIUM CHANNELS AND TO INHIBIT PHOSPHODIESTERASE TYPE 3 ACTIVITY

Appl. No.: 10/679,303

Filing Date: 10/07/2003

Examiner: (not yet assigned)

Art Unit: 1625

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR § 1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Submitted herewith on Forms PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR § 1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR § 1.97 and § 1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR § 1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

RELEVANCE OF EACH DOCUMENT

All of the documents are in English.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 1/30/04

By _____

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(use as many sheets as necessary)				Group Art Unit	1625
				Examiner Name	(not yet assigned)
Sheet	1	of	6	Attorney Docket Number	023597-0110

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U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	U.S. Patent Document Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	4,450,165		Araki et al.	05/22/1984	
	A2	4,568,677		Alker et al.	02/04/1986	
	A3	4,564,619		Tanaka et al.	01/14/1986	
	A4	4,590,195		Alker et al.	05/20/1986	
	A5	4,723,014		Anderson et al.	02/02/1988	
	A6	4,820,842		Anderson et al.	04/11/1989	
	A7	5,100,892		Wheeler et al.	03/31/1992	
	A8	5,258,519		Wheeler et al.	11/02/1993	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

NON PATENT LITERATURE DOCUMENTS

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	A9	FOSSHEIM, "Crystal Structure of the Dihydropyridine Ca^{2+} Antagonist Felodipine. Dihydropyridine Binding Prerequisites Assessed from Crystallographic Data," *J. Med. Chem.*, Vol. 29, pp. 305-307, (1986), American Chemical Society	
	A10	TAMAZAWA et al., "Stereoselectivity of a Potent Calcium Antagonist, 1-Benzyl-3-pyrrolidinyl Methyl 2,6-Dimethyl-4-(*m*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate," *J. Med. Chem.*, Vol. 29, pp 2504-2511, (1986) American Chemical Society	
	A11	SUNKEL et al., "Synthesis of 3-[2,3-Dihydro-1,1,3-trioxo-1,2-benzisothiazol-2-yl]alkyl] 1,4-Dihydropyridine-3,5-dicarboxylate Derivatives as Calcium Channel Modulators," *J. Med. Chem.*, Vol. 35, pp. 2407-2414, (1992), American Chemical Society	
	A12	ARROWSMITH et al., "Long-Acting Dihydropyridine Calcium Antagonists. 1. 2-Alkoxymethyl Derivatives Incorporating Basic Substituents," *J. Med. Chem.*, Vol. 29, pp. 1696-1702, (1986), American Chemical Society, UK	
	A13	ALKER, et al., "Long-Acting Dihydropyridine Calcium Antagonists. 5. Synthesis and Structure-Activity Relationships for a Series of 2-[[(*N*-Substituted-heterocyclyl)ethoxy]methyl]-1,4-dihydropyridine Calcium Antagonists," *J. Med. Chem.*, Vol. 33, pp. 1805-1811, (1990), American Chemical Society, UK	
	A14	ROVNYAK, et al., "Active Conformation of 1,4-Dihydropyridine Calcium Entry Blockers. Effect of Size of 2-Aryl Substituent on Rotameric Equilibria and Receptor Binding," *J. Med. Chem.*, Vol. 34, pp. 2521-2524, (1991), American Chemical Society	
	A15	GOLDMANN, et al., "Synthesis, Pharmacological Effects, and Conformation of 4,4-Disubstituted 1,4-Dihydropyridines," *J. Med. Chem.*, Vol. 33, pp. 1413-1418, (1990), American Chemical Society	

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	A16	ATWAL, et al., "Dihydropyrimidine Calcium Channel Blockers: 2-Heterosubstituted 4-Aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," *J. Med. Chem.*, Vol. 33, pp. 1510-1515, (1990), American Chemical Society	
	A17	ATWAL, et al., "Dihydropyrimidine Calcium Channel Blockers. 2.[1] 3-Substituted-4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," *J. Med. Chem.*, Vol. 33, pp. 2629-2635, (1990), American Chemical Society	
	A18	ALKER, et al., "Long-Acting Dihydropyridine Calcium Antagonists. 4. Synthesis and Structure-Activity Relationships for a Series of Basic and Nonbasic Derivatives of 2-[(2-Aminoethoxy)methyl]-1,4-dihydropyridine Calcium Antagonists," *J. Med. Chem.*, Vol. 33, pp. 585-591, (1990), American Chemical Society	
	A19	NATALE, et al., "Lipophilic 4-Isoxazolyl-1,4-dihydropyridines: Synthesis and Structure-Activity Relationships," *J. Med. Chem.*, Vol. 42, pp. 3087-3093, (1999), American Chemical Society	
	A20	MALHOTRA et al., "Barnidipine," Drugs, Vol. 61, pp. 989-996, (2001), Auckland, New Zealand	
	A21	JOSLYN, et al., "Dimeric 1,4-Dihydropyridines as Calcium Channel Antagonists," *J. Med. Chem.*, Vol. 31, pp. 1489-1492, (1988), American Chemical Society	
	A22	ALKER, et al., "Long-Acting Dihydropyridine Calcium Antagonists. 3. Synthesis and Structure-Activity Relationships for a Series of 2-[(Heterocyclylmethoxy)methyl] Derivatives," *J. Med. Chem.*, Vol. 32, pp. 2381-2388, (1989), American Chemical Society	
	A23	NOVINSON, et al., "3-Substituted 5,7-Dimethylpyrazolo[1,5-α]pyrimidines, 3',5'-Cyclic-AMP Phosphodiesterase Inhibitors," *J. Med. Chem.*, Vol. 17, No. 6, pp. 645, 648, (1974)	
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	A25	COATES, et al., "Cyclic Nucleotide Phosphodiesterase Inhibition by Imidazopyridines: Analogues of Sulmazole and Isomazole as Inhibitors of the cGMP Specific Phosphodiesterase," *J. Med. Chem.*, Vol. 36, pp. 1387-1392, (1993), American Chemical Society	
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	A27	MOOS, et al., "Cardiotonic Agents. 8. Selective Inhibitors of Adenosine 3',5'-Cyclic Phosphate Phosphodiesterase III. Elaboration of a Five-Point Model for Positive Inotropic Activity," *J. Med. Chem.*, Vol. 30, pp. 1963-1972, (1987), American Chemical Society	
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	A30	SIRCAR, et al., "Cardiotonic Agents, 7. Inhibition of Separated Forms of Cyclic Nucleotide Phosphodiesterase from Guinea Pig Cardiac Muscle by 4,5-Dihydro-6-[4-(1-*H*-imidazol-1-yl)phenyl]-3(2*H*)-pyridazinones and Related Compounds. Structure-Activity Relationships and Correlation with in Vivo Positive Inotropic Activity," *J. Med. Chem.*, Vol. 30, pp. 1955-1962, (1987), American Chemical Society	
	A31	SIRCAR, et al., "Cardiotonic Agents. 9. Synthesis and Biological Evaluation of a Series of (*E*)-4,5-Dihydro-6-[2-[4-(1*H*-imidazol-1-yl)phenyl]ethenyl]-3(2*H*)-pyridazinones: A Novel Class of Compounds with Positive Inotropic, Antithrombotic, and Vasodilatory Activities for the Treatment of Congestive Heart Failure," *J. Med. Chem.*, Vol. 32, pp. 342-350, (1989), American Chemical Society	
	A32	GARST, et al., "Inhibition of Separated Forms of Phosphodiesterases from Pig Coronary Arteries by Uracils and by 7-Substituted Derivatives of 1-Methyl-3-isobutylxanthine," *J. Med. Chem.*, Vol. 19, No. 4, pp. 499-503, (1976),	
	A33	GOODSELL, et al., "8-Substituted Theophyllines. *In Vitro* Inhibition of 3'-5'-Cyclic Adenosine Monoposphate Phosphodiesterase and Pharmacological Spectrum in Mice," *Journal of Medicinal Chemistry*," Vol. 14, No. 12 pp. 1202-1205, (1971)	

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Sheet | 4 | of | 6

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	A34	MEANWELL, et al., "Inhibitors of Blood Platelet cAMP Phosphodiesterase. 2. Structure-Activity Relationships Associated with 1,3-Dihydro-2*H*-imidazo[4,5-*b*]quinolin-2-ones Substituted with Functionalized Side Chains," *J. Med. Chem.*, Vol. 35, pp. 2672-2687, (1992), American Chemical Society	
	A35	WELLS, et al., "Inhibition of Separated Forms of Cyclic Nucleotide Phosphodiesterase from Pig Coronary Arteries by 1,3-Disubstituted and 1,3,8-Trisubstituted Xanthines," *J. Med. Chem.*, Vol. 24, pp. 954-958, (1981), American Chemical Society	
	A36	SCHNELLER, et al., "Inhibition of Cyclic Nucleotide Phosphodiesterases fro Pig Coronary Artery by Benzo-Separated Analogues of 3-Isobutyl-1-methylxanthine," *J. Med. Chem.*, Vol. 29, pp. 972-978, (1986), American Chemical Society	
	A37	BUCHMAN, et al., "Imidazole Derivatives as Inhibitors of Cyclic Nucleotide Phosphodiesterases," *J. Med. Chem.*, Vol. 17, No. 11 pp. 1168-1173, (1974)	
	A38	LAMPE, et al., "(Imidazolylphenyl)pyrrol-2-one Inhibitors of Cardiac cAMP Phosphodiesterase," *J. Med. Chem.*, Vol. 36, pp. 1041-1047, (1993), American Chemical Society	
	A39	SIRCAR, et al., "Cardiotonic Agents. 3. Synthesis and Biological Activity of Novel 6-(Substituted 1*H*-imidazol-4(5)-yl)-3(2*H*)-pyridazinones," *J. Med. Chem.*, Vol. 29, pp. 261-267, (1986), American Chemical Society	
	A40	NOVINSON, et al., "2-(Alkylthio)-1,2,4-triazolo[1,5-*a*]pyrimidines as Adenosine Cyclic 3',5'-Monophosphate Phosphodiesterase Inhibitors with Potential as New Cardiovascular Agents," *J. Med. Chem.*, Vol. 25, pp. 420-426, (1982) American Chemical Society	
	A41	SIRCAR, et al., "Cardiotonic Agents. 4. Synthesis and Biological Evaluation of N-Substituted 2,4,4a,5-Tetrahydro-3*H*-indeno[1,2-*c*]pyridazin-3-ones: Rigid Structures Derived from CI-930 and Analogues," *J. Med. Chem.*, Vol. 29, pp. 2142-2148, (1986), American Chemical Society	
	A42	SIRCAR, et al., "Cardiotonic Agents. 2. Synthesis and Structure-Activity Relationships of 4,5-Dihydro-6-[4-(1*H*-imidazol-1-yl)phenyl]-3(2*H*)-pyridazinones: A New Class of Positive Inotropic Agents," *J. Med. Chem.*, Vol. 28, pp. 1405-1413, (1985), American Chemical Society	

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	A43	HARRISON, et al., "Novel Alkaline Ring Cleavage of 2-Phenyl-3-hydroxythieno[2,3-*b*]quinoline 1,1-Dioxide, a Potent inhibitor of Cyclic Adenosine 5'-Monophosphate Phosphodiesterase," *J. Org. Chem.*, Vol. 44, No. 17, pp. 2977-2979, (1979), American Chemical Society	
	A44	MEANWELL, et al., "Inhibitors of Blood Platelet cAMP Phosphodiesterase. 3. 1,3-Dihydro-*2H*-imidazo[4,5-*b*]quinolin-2-one Derivatives with Enhanced Aqueous Solubility," *J. Med. Chem.*, Vol. 35, pp. 2688-2696, (1992), American Chemical Society	
	A45	SIRCAR, et al., "Calcium Channel Blocking and Positive Inotropic Activities of Ethyl 5-Cyano-1,4-dihydro-6-methyl-2[(phenylsulfonyl)methyl]-4-aryl-3-pyridine-carboxylate and Analogues. Synthesis and Structure-Activity Relationships," *J. Med. Chem.*, Vol. 34, pp. 2248-2260, (1991), American Chemical Society	
	A46	COATES, et al., "1,4-Bis(3-oxo-2,3-dihydropyridazin-6-yl)benzene Analogues: Potent Phosphodiesterase Inhibitors and Inodilators," *J. Med. Chem.*, Vol. 33, pp. 1735-1741, (1990), American Chemical Society	
	A47	SIRCAR, et al., "1,2-Dihydro-5-[4-(1*H*-imidazol-1-yl)phenyl]-6-methyl-2-oxo-3-pyridinecarbonitriles and Related Compounds. Synthesis and Inotropic Activity," *J. Med. Chem.*, Vol. 30, pp. 1023-1029, (1987),	
	A48	NOVINSON, et al., "Adenosine Cyclic 3',5'-Monophosphate Phosphodiesterase Inhibitors. 2. 3-Substituted 5,7-Dialkylpyrazolo[1,5-*a*]pyrimidines," *Journal of Medicine Chemistry*, Vol. 18, No. 5, pp. 460-464	
	A49	SAWANISHI, et al., "Selective Inhibitors of Cyclic AMP-Specific Phosphodiesterase: Heterocycle-Condensed Purines," *J. Med. Chem.*, Vol. 40, pp. 3248-3253, (1997), American Chemical Society	
	A50	ARROWSMITH, et al., "Long Acting Dihydropyridine Calcium Antagonists. 2. 2-[2-Aminoheterocycloethoxy]methoxy]methyl Derivatives," *J. Med. Chem.*, Vol. 32, pp. 562-568, (1989), American Chemical Society	
	A51	NISHI, et al., "Studies on 2-Oxoquinoline Derivatives as Blood Platelet Aggregation Inhibitors. III. *N*-Cyclohexyl-*N*(2-hydroxyethyl)-4-(1,2-dihydro-2-oxo-6-quinolyloxy)-butyramide and Related Compounds," *Chem. Pharm. Bull.*, Vol. 31, No. 3 pp. 852-860, (1983)	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	10/679,303
Date Submitted: January 30, 2004				**Filing Date**	10/07/2003
				First Named Inventor	Gregory S. Hamilton
(use as many sheets as necessary)				Group Art Unit	1625
				Examiner Name	(not yet assigned)
Sheet	6	of	6	Attorney Docket Number	023597-0110

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	A52	LUGNIER, et al., "Substituted carbostyrils as inhibitors of cyclic AMP phosphodiesterase," *Eur. J. Med. Chem. – Chim. Ther.*, Vol. 20, No. 2 pp. 121-125, (1985)	
	A53	JONES, et al., "Inhibitors of Cyclic AMP Phosphodiesterase. 1. Analogues of Cilostamide and Anagrelide," *J. Med. Chem.*, Vol. 30, pp. 295-303, (1987), American Chemical Society	
	A54	Results of computer search in *Chemical Abstracts Registry*, comprising Parts I to IV	

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